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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/047,072	01/15/2002	Ralph M. Steinman	MER-011CN/112917-144	7452

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EXAMINER	
EWOLDT, GERALD R	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 07/28/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

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Office Action Summary	Application No.	Applicant(s)	
	10/047,072	STEINMAN ET AL.	
	Examiner	Art Unit	
	G. R. Ewoldt, Ph.D.	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 April 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1-6 and 10-12* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1-6 and 10-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. A request for continued examination (RCE) under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's amendments and remarks filed 4/19/04 have been entered.

2. Claims 1-6 and 10-12 are being acted upon.

3. In view of Applicant's amendment and remarks, filed 4/19/04, the previous rejection under the second paragraph of 35 U.S.C. 112 regarding the recitation of "pluripotential cells" has been withdrawn. As now recited in the claims, "pluripotential cells" would include any cell of a not fixed or plastic developmental state having the potential of expressing either macrophage or dendritic cell (DC) characteristics. Additionally, the previous rejections under 35 U.S.C. 102 (b) and (e) have also been withdrawn.

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1-6 and 10-12 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

Specifically, there is insufficient written description to show that Applicant was in possession of a factor in which to culture pluripotential cells which would cause them to express characteristics of DCs, for the reasons of record as set forth in the papers mailed 4/02/03 and 1/16/04.

Applicant's arguments, filed 4/19/04, have been fully considered but they are not persuasive. Applicant argues that "Applicants' specification has provided two sources for the factor, namely conditioned medium and fixed *Staphyloccus aureus* (SACS) (see, e.g., page 47, line 14 through page 54, line 25). Thus, Applicants respectfully aver that the ordinally skilled artisan would conclude, upon reading the specification, that Applicants possessed the claimed invention at the time the Application was filed." Applicant further argues that current caselaw does not require that Applicant identify said factor and points to *Enzo Biochem v. Genprobe Inc.*, 323 F.3d 956, 965 (Fed. Cir. 2002) for support.

As set forth previously, it is clear that Applicant does not know (or did not know at the time of filing) the identity of the "factor" of the instant claims. The specification does, however, disclosed two methods of obtaining said factor. It remains the Examiner's position that the specification's limited description of two ways of obtaining stable, mature DCs is insufficient for the claimed method wherein some unknown "factor" is asserted to be responsible. In the first example the specification discloses that the "factor" of the claims can be found in "conditioned medium" (CM) comprising RPMI supplemented with gentamycin, HEPES, and FCS or autologous plasma (page 28), in which T cell-depleted PBMC are cultured on Ig coated plates (page 29). Alternatively, stable, mature DCs are generated by adding SACS (Pansorbin) to T cell-depleted cultures of DC after 7 days (page 34). Applicant's conclude (but fail to demonstrate) that the stable, mature DCs generated by their method are made stable and mature by the "factor" of the instant claims. It could just as well be concluded that the DCs generated by the method of the claims are a result of the specific culture conditions or manipulations disclosed in the specification. Thus, it is the Examiner's position that Applicant has not only failed to adequately describe the "factor" of the instant claims, Applicant has failed to demonstrate that said "factor" even exists.

Regarding Applicant's citing of *Enzo*, said case could just as well be used to support the Examiner's position. For example, the court held, "we conclude that proof of a reduction to practice, absent an adequate description in the specification of what is reduced to practice, does not serve to describe or identify the invention for purposes of § 112, ¶ 1. As with "possession," proof of a reduction to practice may show priority of invention or allow one to antedate a reference, but it does not by itself provide a written description in the patent specification." This holding would seem to better support the

Examiner's position than Applicant's. Regardless, it is made clear in the conclusions of the case that the findings are most relevant to cases involving 112, first paragraph, written description questions as they regard deposits of DNA, "this case has taken us into new territory and we have held, as a matter of first impression, that reference in a patent specification to a deposit of genetic material may suffice to describe that material". There are no deposit issues in the instant case, thus, the findings of *Enzo* are of little relevance to the questions at hand of whether or not the "factor" of the instant claims exists and if so, is it adequately described. Also consider the fact that with deposited biological samples, (e.g., DNA, hybridomas, etc.), claims reciting the deposited sample *only* encompass inventions comprising or employing the deposited sample. It is clear from the prosecution of the instant case that Applicant in no way intends to limit the scope of the claimed method to encompass only the specific conditions of the Examples of the instant specification.

Finally note that even Inventor Steinman, some 3 years post effective filing date, questions whether an actual "factor" exists. In *Fundamental Immunology* (1999) the Inventor states, "No one cytokine is responsible for DC maturation, and it is possible that a combination is required to induce the many different features of DCs" (page 558).

6. Claims 1-6 and 10-12 stand rejected under 35 U.S.C. § 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed for the reasons of record as set forth in the paper mailed 1/16/04. This is a new matter rejection.

The specification and the claims as originally filed do not provide support for the invention as now claimed, specifically, a method ... comprising ... decreased CD115 expression and decreased CD32 expression relative to the pluripotential cells.

Applicant now indicates that support for the new limitations can be found at pages 17, 55, and 56, as well as Figure 7.

Applicant's arguments, filed 4/19/04, have been fully considered but they are not persuasive. No disclosure regarding CD115 or CD32 expression has been found at page 17. Page 55 discloses that in one experiment CD115 expression is lost and CD32 is downregulated. There is no disclosure regarding CD115 or

CD32 expression at page 56. The legend of Figure 7 discloses that, again, in a single experiment, mature DCs "lose CD115 expression". Applicant is advised that results of individual experiments provide insufficient written description for generic claims. Thus, a disclosure that when one type of DC cultured in one specific way a certain cell surface marker is lost, is an insufficient description of a generic method encompassing all types of DCs produced in any way. Also note that the mature DCs of the disclosure are never compared to pluripotential cells as recited in the claims. Accordingly the rejection is proper and has been maintained.

7. The following are new grounds of rejection.

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
> (e) the invention was described in-
> (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or
> (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

9. Claims 1-6 and 10-12 are rejected under 35 U.S.C. 102(e) as being clearly anticipated by U.S. Patent No. 5,994,126 (of record) as evidenced by Kiertscher et al. (1996).

The '126 patent teaches an *in vitro* method of producing DCs comprising culturing pluripotential cells comprising monocytes (which are inherently $CD14^+$) or mononuclear cells (both components of PBMCs) in about 200U/ml to about 2000U/ml of a "factor" comprising GM-CSF and additionally IL-4 (see particularly column 16, lines 43-45 and Example 1). Note that Claims 11 and 12 merely recite well known properties inherent to DCs, i.e., high level expression of MHC molecules and the capacity to stimulate resting T cells. Kiertscher et al. demonstrates that PBMC cultured in GM-CSF and IL-4 (Figure 1),

the method of the '126 patent, results in the DCs of the instant claims, e.g., DCs with increased CD83 expression (Table I).

The reference clearly anticipates the claimed invention.

10. Claims 1-6 and 10-12 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Romani et al. (1994, of record)as evidenced by Caux et al. (of record).

Romani et al. teaches an *in vitro* method of producing DCs comprising culturing pluripotential cells comprising monocytes (which are inherently $CD14^+$) or mononuclear cells (both components of PBMCs) in about 200U/ml to about 2000U/ml of a "factor" comprising GM-CSF and additionally TNF-α (see particularly page 84, **Materials and Methods**). Note that Claims 11 and 12 merely recite well known properties inherent to DCs, i.e., high level expression of MHC molecules and the capacity to stimulate resting T cells. Caux et al. (1996) demonstrates that pluripotential cells cultured in GM-CSF and TNF-α (Materials and Methods), the method of Romani et al., results in the DCs of the instant claims, e.g., DCs with increased CD83 and CD86 expression (Figure 5).

Applicant's arguments traversing similar rejections under 35 U.S.C. 102, filed 4/19/04, have been fully considered but they are not persuasive. Applicant argues that, "these references [the '126 patent and Romani et al.] describe methods to generate immature dendritic cells, the present Application teaches methods for generating mature dendritic cells from either immature dendritic cells or pluripotential cells... The methods described by the '126 patent and by Romani merely result in the production of immature dendritic cells, that is, a cell that, once removed from the cytokines used to produce it, reverts back to a pluripotential cell having characteristics similar to macrophages".

Applicant's arguments fail to recognize that the invention of the claims is not the invention Applicant traverses. The claims simply recite a method of producing a DC expressing increased CD83 or CD86, or decreased CD115 or CD32. Applicant's arguments involve mature DCs, yet the term "mature dendritic cells" does not appear in the claims. Applicant further argues that the DCs of the claims are "stable mature dendritic cells", yet Applicant again fails to claim the limitation. Note that the limitations of independent Claim 1 merely require that just one of the listed CD markers show a change. Accordingly, the prior art meets the limitations of the claims

11. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

12. Claims 1-6 and 10-12 stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically:

A) The term "cells having the potential to express macrophage...characteristics" is vague and indefinite as the term "macrophage characteristics" is not defined in the specification.

13. Claims 1-6 and 10-12 stand rejected under 35 U.S.C. § 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed. This is a new matter rejection.

The specification and the claims as originally filed do not provide support for the invention as now claimed,

"An in vitro method for producing dendritic cells from pluripotential cells, comprising contacting the pluripotential cells having the potential of expressing either macrophage or dendritic cell characteristics with a factor for a time sufficient for the pluripotential cells to mature and express a characteristic of dendritic cells, wherein the characteristic is selected from the group consisting of increased CD83 expression, increased CD86 expression, decreased CD115 expression, and decreased CD32 expression relative to the pluripotential cells", as recited in Claim 1.

Specifically, the specification discloses a method for producing <u>stable mature</u> dendritic cells having the potential of expressing either macrophage or dendritic cell characteristics, but not the broader, method for producing [any type of] dendritic cells having the potential of expressing either macrophage or dendritic cell characteristics. Likewise, the specification discloses a method of producing mature DCs from immature DCs, said mature DCs comprising increased CD83 expression, increased CD86 expression, decreased CD115 expression, or decreased CD32 expression, but not the broader method of the claim.

Applicant indicates that support for the new amendment can be found at page 6 of the specification but support for the limitations as set forth above has not been found.

14. No claim is allowed.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Gerald Ewoldt whose telephone number is (571) 272-0843. The examiner can normally be reached Monday through Thursday from 7:30 am to 5:30 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841.

15. **Please Note**: Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). Inquiries of a general nature may also be directed to the Technology Center 1600 Receptionist at (571) 272-1600.

1/20/04

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